

A BIONIC APPROACH TO CARDIOVASCULAR REGULATION: BIONIC ARTERIAL BAROREFLEX SYSTEM

M. Sugimachi¹, T. Sato², T. Kawada¹, M. Inagaki^{1,3}, K. Sunagawa¹

¹Department of Cardiovascular Dynamics, National Cardiovascular Center Research Institute, Suita, Japan

²Department of Physiology II, Kochi Medical School, Nankoku, Japan

³Japan Science and Technology Corporation, Kawaguchi, Japan

Abstract- A bionic system is an artificial device, integrated into natural human physiology by communicating with native regulatory system. This can functionally operate as if it were a part of the body. Bionic systems can be realized only with the knowledge of detailed characteristics of native system. We made use of “white-noise approach” and have succeeded in functionally identifying the native arterial baroreflex. Using thus identified characteristics, we developed a bionic baroreflex system. Animal experiments in rats revealed that the bionic baroreflex system can stabilize pressure against hypotensive stimuli such as head-up tilt even without the native baroreflex system.

Keywords- White noise approach, Transfer function, Bionic baroreflex system*

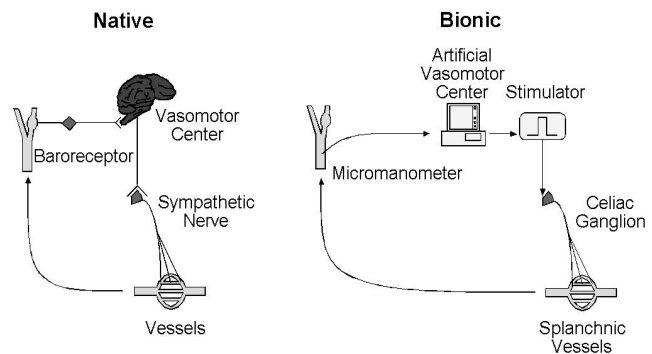


Fig. 1. Schema of bionic arterial baroreflex system. In animals without functional baroreflex system, one can restore baroreflex function by measuring blood pressure with micromanometer and by stimulating celiac with the knowledge of system characteristics.

I. INTRODUCTION

A bionic system is an artificial device, integrated into natural human physiological systems by communicating with the native regulatory system, especially through the nervous system. Bionic systems can functionally operate as if they were a part of the body. These bionic systems open up a new therapeutic strategy against various cardiovascular diseases by restoring the lost function, or by modifying the abnormally functioning regulatory system.

Besides the methods to interface with the nervous system, development of bionic systems requires the knowledge of detailed characteristics of native system. Unlike artificial systems, native systems have a number of factors contributing to the complexity such as history-dependence, feedback nature, multiplicity and interaction of inputs, nonlinearity, and distributed nature. To overcome these, we made use of “white-noise approach” and have

succeeded in functionally identifying the native arterial baroreflex with the precision one can reproduce native system artificially [1, 2, 3]. Using thus identified characteristics, we developed a bionic baroreflex system (Fig. 1) [4, 5] and examined if the bionic baroreflex system can stabilize pressure against hypotensive stimuli even in animals without functional baroreflex system.

II. METHODOLOGY

A. Functional identification with white-noise approach

In anesthetized rats with halothane, both carotid sinuses were vascularly isolated. Aortic depressor nerves and vagal nerves were cut bilaterally. We connected a high-fidelity piston pump to control carotid sinus pressure (CSP) as needed. We recorded CSP, cardiac sympathetic nerve activity (SNA), and systemic arterial pressure (SAP) simultaneously at sampling frequency of 100 Hz and resolution of 12 bits for 20 minutes while randomly perturbing sinus pressure. Nerve activity was quantified by smoothing the fully rectified signals. These signals were saved on hard disk for subsequent analysis. Transfer function (H_{total}) of total native baroreflex system was obtained.

Similarly we recorded blood pressure while stimulating sympathetic nerves at the celiac ganglia randomly. We

This study was supported by Grants-in-Aid for Scientific Research (B 11694337, B 12557066, C 12670716) and for Encouragement of Young Scientists (13770378, 13770379) from the Japan Society for the Promotion of Science, by Research Grants for Cardiovascular Diseases (11C-3) and a Health Sciences Research Grant for Advanced Medical Technology from the Ministry of Health and Welfare of Japan, Research and Development Grant for Applying Advanced Computational Science and Technology from Japan Science and Technology Corporation, Program for Promotion of Fundamental Studies in Health Science of the Organization for Pharmaceutical Safety and Research, Ground-Based Research Grant for the Space Utilization from National Space Development Agency of Japan and Japan Space Forum.

Report Documentation Page

Report Date 25 Oct 2001	Report Type N/A	Dates Covered (from... to) -
Title and Subtitle A Bionic Approach to Cardiovascular Regulation: Bionic Arterial Baroreflex System		Contract Number
		Grant Number
		Program Element Number
Author(s)		Project Number
		Task Number
		Work Unit Number
Performing Organization Name(s) and Address(es) Department of Cardiovascular Dynamics National Cardiovascular Center Research Institute Suita, Japan		Performing Organization Report Number
Sponsoring/Monitoring Agency Name(s) and Address(es) US Army Research, Development & Standardization Group (UK) PSC 802 Box 15 FPO AE 09499-1500		Sponsor/Monitor's Acronym(s)
		Sponsor/Monitor's Report Number(s)
Distribution/Availability Statement Approved for public release, distribution unlimited		
Supplementary Notes Papers from 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society, October 25-26, 2001 held in Istanbul, Turkey. See also ADM001351 for entire conference on cd-rom.		
Abstract		
Subject Terms		
Report Classification unclassified	Classification of this page unclassified	
Classification of Abstract unclassified	Limitation of Abstract UU	
Number of Pages 3		

obtained transfer function (H_{effect}) of the effector of native baroreflex. This transfer function strikingly resembles that from SNA and SAP obtained with CSP perturbation.

From these transfer functions, we calculated the dynamic characteristics (H_{bionic}), by dividing H_{total} by H_{effect} , that are necessary for the bionic baroreflex system.

B. Functional replacement of baroreflex system with bionic approach

We used the same preparation for examining the bionic baroreflex performance as that described in the previous section. Although both carotid sinuses were isolated, pressure regulation under the operation of closed-loop baroreflex can be simulated by equating the sinus pressure to the systemic pressure with the piston pump. We abolished the baroreflex by keeping the sinus pressure constant. The bionic baroreflex was realized by stimulating the celiac ganglia according to the stimulation command. The stimulation command was calculated by convolving the instantaneous sinus pressure with the impulse response of the H_{bionic} . We examined the performance of bionic baroreflex system by imposing head-up tilt on these rats.

III. RESULTS

A. Functional identification with white-noise approach

The left panel of Fig. 2 illustrates an example of time course of random CSP perturbation and SAP changes in response to CSP. Careful observation reveals that SAP decreased when CSP increased though SAP was unresponsive to rapid changes in CSP. Transfer function H_{total} showed low-pass characteristics with the corner frequency of ~ 0.1 Hz. Transfer function H_{effect} similarly showed low-pass characteristics. The resultant H_{bionic} showed

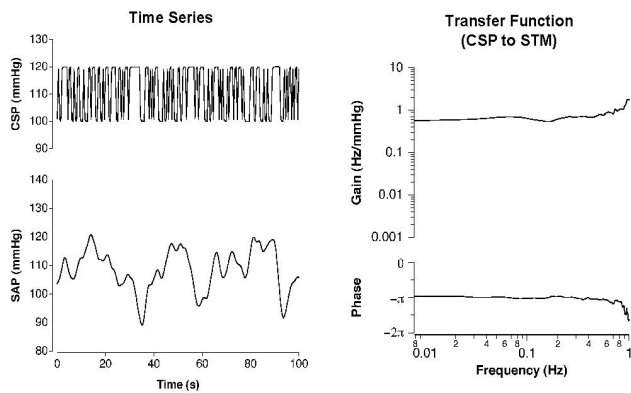


Fig. 2. An example of time course of random sinus pressure (CSP) perturbation and changes in systemic arterial pressure (SAP) in response to CSP (left) and calculated transfer function necessary for the bionic baroreflex system (right). STM, stimulation frequency.

almost all-pass characteristics with some derivative property in the high frequencies (Fig. 2, right).

B. Functional replacement of baroreflex system with bionic approach

As shown in Fig. 3, systemic pressure decreases dramatically in 10 seconds (52 ± 5 mmHg, $n=16$) by the abrupt head-up tilt in rats with no functional baroreflex system. When we activate the bionic baroreflex system, thanks to the abrupt onset of celiac stimulation and increase in stimulation frequency, pressure considerably recovered in 10 seconds and decreased significantly less (15 ± 6 mmHg). The time course and the amplitude of the hypotension with a bionic baroreflex were indistinguishable with a native one.

IV. DISCUSSION

Bionic medicine is a novel therapeutic strategy to treat various diseases by intervening native physiological system with bionic devices. Because the abnormality in cardiovascular regulation contributes to the maintenance of different cardiovascular diseases, this approach is likely to have a large number of applications in cardiology.

We have shown in this study that the bionic approach is feasible in treating orthostatic hypotension occurring as a result of central baroreflex failure. This system became possible with the detailed identification of the native system. In identifying the system we avoided to cut the system into pieces; we treated the system as a whole integrated one. This is in contrast with recent reductionist approaches in medicine and biology. We believe that this integrated approach is essential in developing a number of novel therapeutic devices to save patients suffering from various diseases.

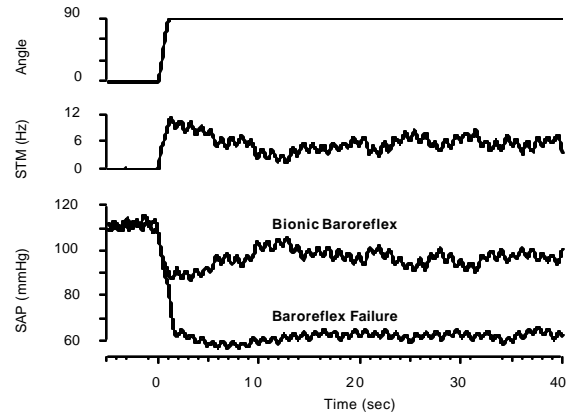


Fig. 3. Changes in systemic arterial pressure (SAP) before and after abrupt head-up tilt (increase in angle) without functional baroreflex (baroreflex failure) and with a bionic baroreflex. Changes in stimulation frequency (STM) of celiac ganglion for a bionic baroreflex is also shown.

V. CONCLUSION

By functionally identifying the arterial baroreflex system and by replacing it with the bionic system, we succeeded in reproducing the static as well as dynamic characteristics of the native baroreflex by an artificial device. The bionic medicine will pioneer the new therapeutic strategy not only in cardiology but also in various fields of medicine

REFERENCES

- [1] Y. Ikeda, T. Kawada, M. Sugimachi, O. Kawaguchi, T. Shishido, T. Sato, et al., "Neural arc of baroreflex optimizes dynamic pressure regulation in achieving both stability and quickness," *Am. J. Physiol. (Heart and Circ. Physiol.)*, vol. 271, pp. H882-H890, 1996.
- [2] T. Kawada, Y. Ikeda, M. Sugimachi, T. Shishido, O. Kawaguchi, et al., "Bidirectional augmentation of heart rate regulation by autonomic nervous system in rabbits," *Am. J. Physiol. (Heart and Circ. Physiol.)*, vol. 271, pp. H288-H295, 1996.
- [3] Y. Ikeda, M. Sugimachi, T. Yamasaki, O. Kawaguchi, T. Shishido, T. Kawada, et al., "Explorations into development of a neurally regulated cardiac pacemaker," *Am. J. Physiol. (Heart and Circ. Physiol.)*, vol. 269, pp. H2141-H2146, 1995.
- [4] T. Sato, T. Kawada, T. Shishido, M. Sugimachi, J. Alexander, Jr., and K. Sunagawa, "Novel therapeutic strategy against central baroreflex failure. A bionic baroreflex system," *Circulation*, vol. 100, pp. 299-304, 1999.
- [5] T. Sato, T. Kawada, M. Inagaki, T. Shishido, H. Takaki, M. Sugimachi, et al. "New analytic framework for understanding sympathetic baroreflex control of arterial pressure," *Am. J. Physiol. (Heart and Circ. Physiol.)*, vol. 276, pp. H2251-H2261, 1999.